

Bioinformatics

CS300

Chap 3

**Sequence Alignment:
The Needleman-Wunsch algorithm**

Week5, Deck 1

Fall 2022

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Needleman-Wunsch Algorithm Background

- Global Alignment: Used to determine which parts of a sequence (inside the sequence) are shared (common) with another sequence.
- Developed by Saul B. Needleman and Christian D. Wunsch in 1970.
- Dynamic programming to find optimal solution for matching the characters of the two sequences.



Terms

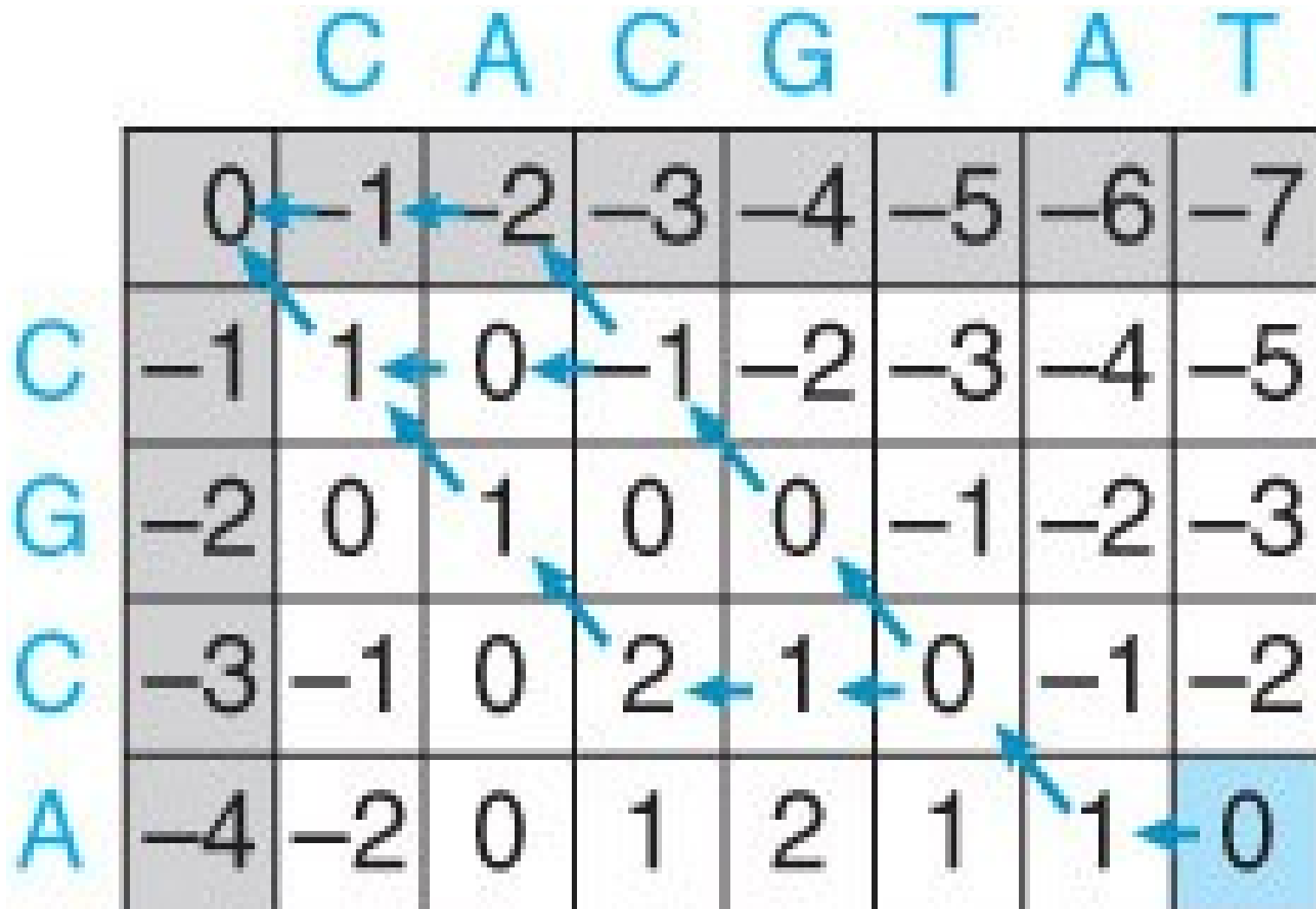
- Alignment is divided up into sub problems
- Solutions are scored; the best solutions for char by char comparison are kept in the overall solution.
- **Match** – bases of each sequence at position ARE same
- **Mismatch** – bases of each sequence at position are NOT same
- **Gap** – bases are not the same, some insert or deletion may have occurred.

AGGCTATCACCTGACCTCCAGGCCGATGCCC
TAGCTATCACGACCGCGGTCGATTGCCCCGAC

–AGGCTATCACCTGACCTCCAGGCCGA––TGCCC––
TAG–CTATCAC––GACCGC––GGTCGATTGCCCCGAC



Global Pairwise Alignment: Needleman-Wunsch



Algorithm

	C	A	C	G	T	A	T	
C	0	-1	-2	-3	-4	-5	-6	-7
G	-1	1	0	-1	-2	-3	-4	-5
C	-2	0	1	0	0	-1	-2	-3
A	-3	-1	0	2	1	0	-1	-2
T	-4	-2	0	1	2	1	1	0

- Create N x M matrix and place each sequence along one axis
- Place score 0 at the up-left corner
- Fill in 1st row & column with gap penalty multiples (here, gap penalty is -1)
- Fill in the matrix with max value of 3 possible moves:
 - Vertical move: Score + gap penalty
 - Horizontal move: Score + gap penalty
 - Diagonal move: Score + match/mismatch score
- To reconstruct the optimal alignment, trace back where the max at each step came from, stop when hit the origin.

For each Element: Three Calculations

- Recursion, based on the principle of optimality:

$$F_{ij} = \max(F_{i-1,j-1} + S(A_i, B_j), F_{i,j-1} + d, F_{i-1,j} + d)$$

The pseudo-code for the algorithm to compute the F matrix therefore looks like this:

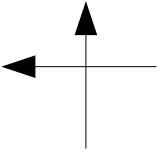
```
for i=0 to length(A)
  F(i,0) ← d*i
for j=0 to length(B)
  F(0,j) ← d*j
for i=1 to length(A)
  for j=1 to length(B)
  {
    Match ← F(i-1,j-1) + S(Ai, Bj)
    Delete ← F(i-1, j) + d
    Insert ← F(i, j-1) + d
    F(i,j) ← max(Match, Insert, Delete)
  }
```



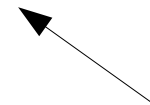
Let's Calculate!

	_	A	T	C	G
_					
T					
C					
A					

- Gap: -1



- Match: 1
- Mismatch: 0

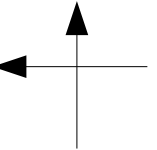




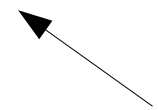
Add The Outer Values

		A	T	C	G
	—				
—	0	-1	-2	-3	-4
T	-1				
C	-2				
A	-3				

- Gap: -1



- Match: 1
- Mismatch: 0

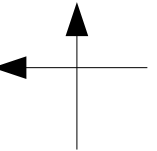




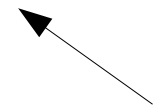
Mismatch: $A \neq T$

	—	A	T	C	G
—	0	-1	-2	-3	-4
T	-1				
C	-2				
A	-3				

- Gap: -1



- Match: 1
- Mismatch: 0



Upperbox:
 $-1 - 1 = -2$

Sidebox:
 $-1 - 1 = -2$

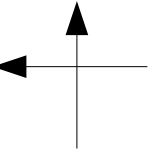
Diag:
 $0 - 0 = 0$



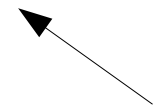
Mismatch: $A \neq T$

	—	A	T	C	G
—	0	-1	-2	-3	-4
T	-1	0			
C	-2				
A	-3				

- Gap: -1



- Match: 1
- Mismatch: 0



Upperbox:
 $-1 - 1 = -2$

Sidebox:
 $-1 - 1 = -2$

Diag:
 $0 - 0 = 0$

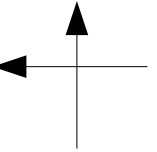
**Max
value**



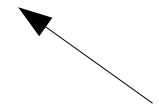
Match: T = T

		A	T	C	G
	—	—	0	-1	-2
T	-1	0	0	-2	-3
C	-2	-3	-4	-5	-6
A	-3	-4	-5	-6	-7

- Gap: -1



- Match: 1
- Mismatch: 0



Upperbox:
 $-2 - 1 = -3$

Sidebox:
 $0 - 1 = -1$

Diag:
 $-1 + 1 = 0$

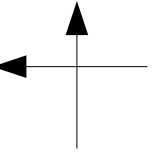
Max
value



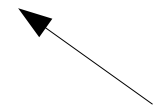
Mismatch: **T** != **C**

		A	T	C	G
	—	0	-1	-2	-3
T	-1	0	0	-1	
C	-2				
A	-3				

- Gap: -1



- Match: 1
- Mismatch: 0



Upperbox:
 $-3 - 1 = -4$

Sidebox:
 $0 - 1 = -1$

**Max
value**

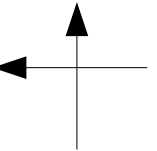
Diag:
 $-2 + 0 = -2$



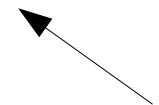
Mismatch: **T** != **G**

	_	A	T	C	G
_	0	-1	-2	-3	-4
T	-1	0	0	-1	-2
C	-2				
A	-3				

- Gap: -1



- Match: 1
- Mismatch: 0



Upperbox:
 $-4 - 1 = -5$

Sidebox:
 $-1 - 1 = -2$

**Max
value**

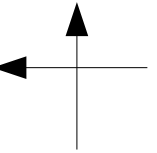
Diag:
 $-3 - 0 = -3$



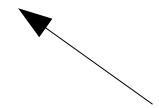
Mismatch: $C \neq A$

		A	T	C	G	
	—	0	-1	-2	-3	-4
T	-1	0	0	-1	-2	
C	-2	-1				
A	-3					

- Gap: -1



- Match: 1
- Mismatch: 0



Upperbox: $0 - 1 = -1$ **Max value**

Sidebox:
 $-2 - 1 = -3$

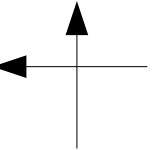
Diag: $-1 + 0 = -1$ **Max value**



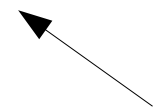
Mismatch: **C** != **T**

		A	T	C	G	
	—	0	-1	-2	-3	-4
T	-1	0	0	-1	-2	
C	-2	-1	0			
A	-3					

- Gap: -1



- Match: 1
- Mismatch: 0



Upperbox:
 $0 - 1 = -1$

Sidebox:
 $-1 - 1 = -2$

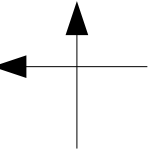
Diag: **0 + 0 = 0** **Max value**



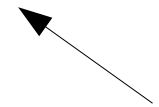
Match: **C** == **C**

		A	T	C	G
	_				
_	0	-1	-2	-3	-4
T	-1	0	0	-1	-2
C	-2	-1	0	1	
A	-3				

- Gap: -1



- Match: 1
- Mismatch: 0



Upperbox:
 $-1 - 1 = -2$

Sidebox:
 $0 - 1 = -1$

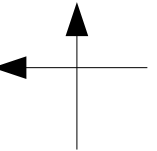
Diag: **0 + 1 = 1** **Max value**



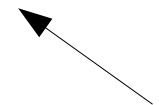
Mismatch: **C** != **G**

	_	A	T	C	G
_	0	-1	-2	-3	-4
T	-1	0	0	-1	-2
C	-2	-1	0	1	0
A	-3				

- Gap: -1



- Match: 1
- Mismatch: 0



Upperbox:
 $-2 - 1 = -3$

Sidebox:
 $1 - 1 = 0$

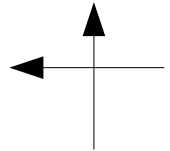
**Max
value**

Diag:
 $-1 - 0 = -1$

Completed With Arrows

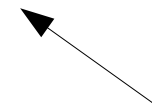
	_	A	T	C	G
_	0	-1	-2	-3	-4
T	-1	0	0	-1	-2
C	-2	-1	0	1	0
A	-3	-1	-1	0	1

• Gap: -1



• Match: 1

• Mismatch: 0



Upperbox:

Sidebox:

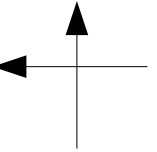
Diag:



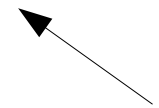
Follow the Arrows Back to Start

	_	A	T	C	G
_	0	-1	-2	-3	-4
T	-1	0	0	-1	-2
C	-2	-1	0	1	0
A	-3	-1	-1	0	1

- Gap: -1



- Match: 1
- Mismatch: 0



Alignment:

A T C G
_ T C A

Follow the Arrows Back To Find the Sequence Alignment

Sequence 1

Sequence 2

Match Score Mismatch Score Gap Score

A	T	C	G
-	T	C	A

Score = 1

		A	T	C	G
	0	-1	-2	-3	-4
T	-1	0 ↖	0 ↖	-1 ←	-2 ←
C	-2	-1 ↖	0 ↖	1 ↖	0 ←
A	-3	-1 ↖	-1 ↖	0 ↖	1 ↖



To Get the Alignment

- With each calculation, we placed an arrow to show how the score was calculated and to give us the actual alignment.

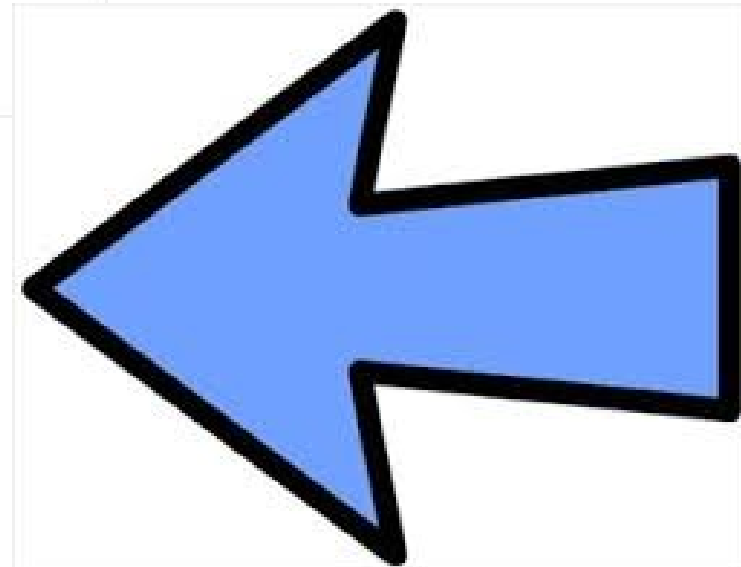
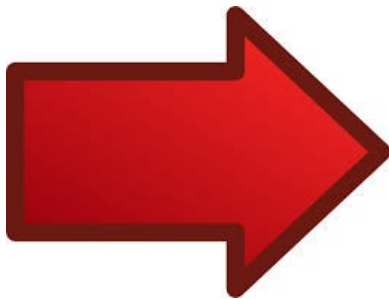
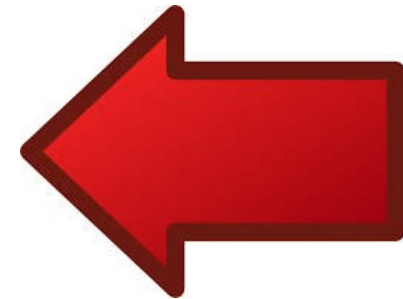
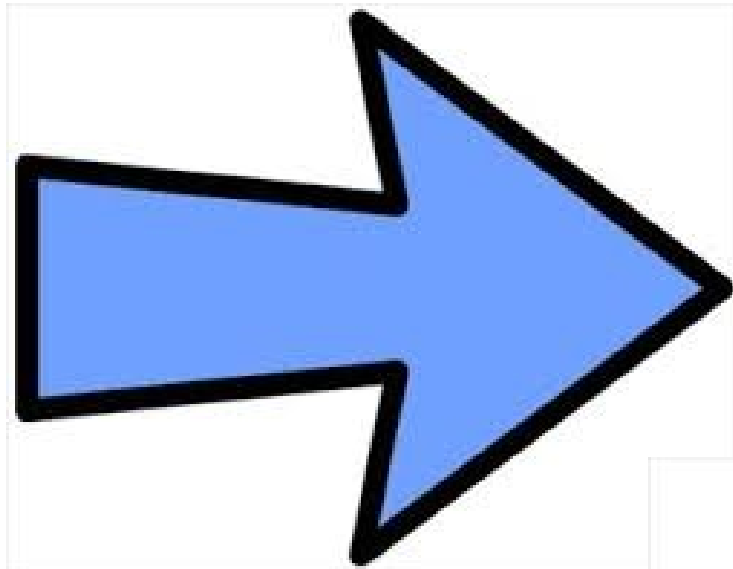
How do we read this output?

Alignment:

A	T	C	G
_	T	C	A



Up Ahead: More Examples of Arrows





Follow the Arrows!

Sequence 1

CGCA

Sequence 2

CACGTAT

Match Score

Mismatch Score

Gap Score

1

0

-1

Compute Optimal Alignment

Clear Path

Custom Path

C A C G T A

C G C - - A

Score = 0

		C	A	C	G	T	A	T
	0	-1	-2	-3	-4	-5	-6	-7
C	-1	1	0	-1	-2	-3	-4	-5
G	-2	0	1	0	0	-1	-2	-3
C	-3	-1	0	2	1	0	-1	-2
A	-4	-2	0	1	2	1	1	0

- S1 = CGCA
- S2 = CACGTAT



Example

Alignment score = 0

Let:

Match = +1

Mismatch = 0

Gap = -1

		C	A	C	G	T	A	T
	0	-1	-2	-3	-4	-5	-6	-7
C	-1	1	0	-1	-2	-3	-4	-5
G	-2	0	1	0	0	-1	-2	-3
C	-3	-1	0	2	1	0	-1	-2
A	-4	-2	0	1	2	1	1	0



Example

Alignment score = 0

Let:

Match = +1

Mismatch = 0

Gap = -1

		C	A	C	G	T	A	T
	0	-1	-2	-3	-4	-5	-6	-7
C	-1	1	0	-1	-2	-3	-4	-5
G	-2	0	1	0	0	-1	-2	-3
C	-3	-1	0	2	1	0	-1	-2
A	-4	-2	0	1	2	1	1	0

CACGTAT

--CGCA--



Example

Alignment score = 0

Let:

Match = +1

Mismatch = 0

Gap = -1

		C	A	C	G	T	A	T
	0	-1	-2	-3	-4	-5	-6	-7
C	-1	1	0	1	-2	-3	-4	-5
G	-2	0	1	0	0	-1	-2	-3
C	-3	-1	0	2	1	0	-1	-2
A	-4	-2	0	1	2	1	1	0

CACGTAT

C - - GCA -



Example

Alignment score = 0

Let:

Match = +1

Mismatch = 0

Gap = -1

		C	A	C	G	T	A	T
	0	-1	-2	-3	-4	-5	-6	-7
C	-1	1	0	-1	-2	-3	-4	-5
G	-2	0	1	0	0	-1	-2	-3
C	-3	-1	0	-2	-1	0	-1	-2
A	-4	-2	0	1	2	1	1	0

CACGTAT

CGC--A-



Example

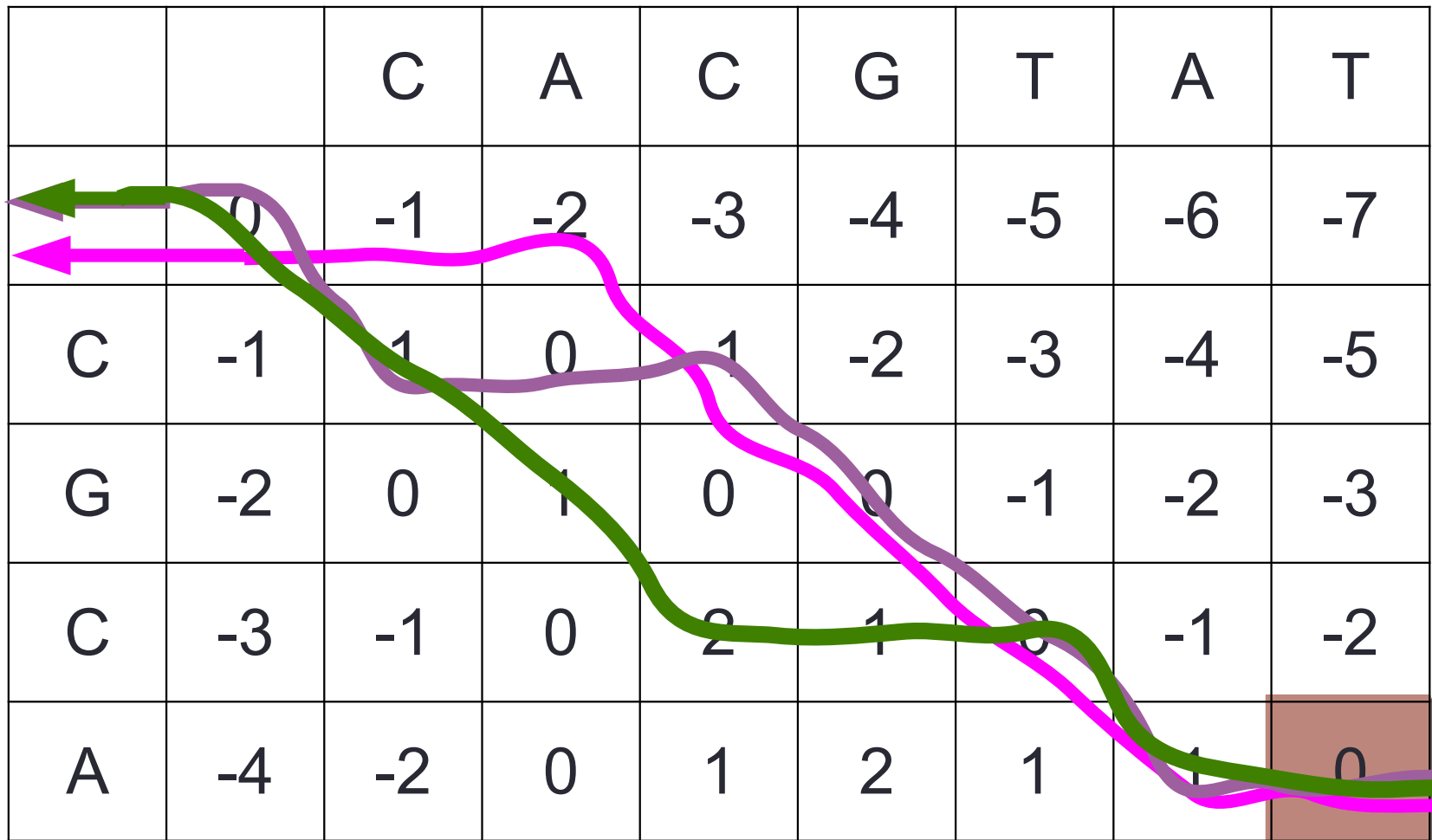
Alignment score = 0

Let:

Match = +1

Mismatch = 0

Gap = -1



CACGTAT
--CGCA-

CACGTAT
C--GCA-

CACGTAT
CGC--A-